

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Application of:

Applicant : Venkatesh et al.
Serial No. : 10/619,924
Filed : July 15, 2003
Title : CONTROLLED RELEASE POTASSIUM CHLORIDE TABLETS
Docket : 451194-095
Examiner : Susan T. Tran
Art Unit : 1615

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Sir:

PRE-APPEAL BRIEF REQUEST FOR REVIEW

This request is filed in response to the final Office action dated February 13, 2007 and is accompanied a Notice of Appeal and the applicable fee. Claims 1-29 remain in this application and have been finally rejected. Applicants submit that the rejections of record are clearly not proper and request that the rejections be withdrawn.

The claims of the present application are directed to a process for preparing a controlled release tablet of potassium chloride and the tablets produced thereby. The process involves blending compressible coated microcapsules of potassium chloride with microcrystalline cellulose (compression aid), a disintegrant and colloidal silicon dioxide and then compressing the blend into tablets. The compressible coated microcapsules can be prepared by microencapsulating potassium chloride crystals with ethylcellulose to form potassium chloride microcapsules and coating the microcapsules with a plasticized polymer. The tablets exhibit a tablet hardness of at least about 14 kP, a friability not more than about 0.3%, and a particular dissolution profile. Furthermore, the tablets rapidly disperse into granules on contact with water.

Claims 1-5, 7-27 and 29 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Gantt et al. WO 01/43725 A1 in view of Sheth et al. US 4,954,349 or Remington. Claims 6 and 28 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Gantt et al. WO 01/43725 A1, in view of Sheth et al. US 4,954,349 or Remington, and Oshlack et al. US 5,472,712. Applicants submit that the rejection of these claims is improper because the Office has failed to carry its burden of establishing a *prima facie* case of obviousness. Applicants submit that the cited references even when combined fail to disclose each and every limitation of the pending claims.

In the final Office action, claims 1-29 were rejected under 35 U.S.C. §112, first paragraph, as failing to comply with the written description requirement. According to the Office action, the specification failed to provide support for the limitation “rapidly disperses into granules on contact with water.” In the response after final, applicants identified several references in the specification supporting the language that was objected to. In the advisory action, the 35 U.S.C. §112, first paragraph, rejection was withdrawn. However, the Examiner failed to identify any reference that disclosed or described tablets rapidly dispersing into granules on contact with water. In fact, the only references to this limitation were with respect to the secondary references. The examiner stated that these references were not relied upon for showing rapid disintegration and/or dispersion into granules. Accordingly, the failure to account for this limitation in the final Office action is improper and the rejection should be withdrawn.

Even if it were assumed for the sake of argument that a *prima facie* case was established, applicants have sufficiently demonstrated the unexpected benefits of the invention sufficient to overcome the *prima facie* case. As discussed in the background of the present application, tablets from the compression blend containing compressible coated potassium chloride microcapsules, microcrystalline cellulose and magnesium stearate as a lubricant failed to rapidly disperse into granules on contact with water. When a disintegrant was incorporated into the tablet composition to promote rapid disintegration in accordance with the teachings of Remington (see Examples 1-3), a tablet weighing about 2 grams exhibited a hardness of less than 5 kP and unacceptable friability. When tablets from the compression blend containing compressible coated potassium chloride microcapsules and microcrystalline cellulose without

including magnesium stearate were compressed into tablets weighing about 2 grams, the tablets exhibited poor friability (greater than 1% loss, see Examples 4-6 and 9). These tablets also failed to meet the disintegration time specification set forth in the present application. Tablets containing compressible coated potassium chloride microcapsules, microcrystalline cellulose, disintegrant and a surfactant which typically improves wetting and thereby promotes tablet disintegration in accordance with the disclosure of Gantt et al. exhibited poor friability even though they had acceptable hardness, drug release profile and disintegration time.

Applicants have determined that compressible coated potassium chloride microcapsules when combined with colloidal silicon dioxide alone or in combination with a surfactant in addition to a disintegrant and microcrystalline cellulose provided tablets that met the specific end use requirements. Neither Gantt nor Remington teaches or suggests the use of colloidal silicon dioxide to provide acceptable tablet hardness, friability, and improved disintegration while also providing for controlled release of the drug.

The final Office action indicated that "the burden has shifted to applicant to show that the compressed tablet of Gantt does not exhibit the claimed properties, because Gantt uses the same ingredients and the same method using the same parameter for the same active." Applicants respectfully submit that such data is present in the application as discussed above. Furthermore, the Office must consider comparative data in the specification which is intended to illustrate the claimed invention in reaching a conclusion with regard to the obviousness of the claims. *In re Margolis*, 785 F.2d 1029, 228 USPQ 940 (Fed. Cir. 1986).

Applicants respectfully submit that this clearly shows that Gantt not only fails to disclose the present invention but also that the present invention is novel and non-obvious over Gantt. In the advisory action the Examiner contends that Gantt discloses using a disintegrant and "clearly suggest including disintegrant to obtain a compressed tablet that is strong with low friability." Applicants respectfully submit that Gantt fails to support the quoted passage. Gantt refers generally to using disintegrants but never discloses that strong tablets of low friability can be formed using disintegrants. The full sentence from Gantt cited by the examiner to support the Examiner's position is: "It was also discovered that microcapsules fluid bed coated with the

plasticized polymeric systems discussed in this patent application could be compressed into strong tablets with low friability without a lubricant (magnesium stearate) or a surfactant (sodium laurel sulfate)." Clearly, this passage refers to the microcapsules being compressible and says nothing about the effect of a disintegrant on the properties of the tablet. Therefore, the present invention provides unexpected benefits that are evidence of the non-obviousness of the invention. For this reason as well, applicants submit that the rejection is in error and should be withdrawn.

In view of the foregoing, it is respectfully submitted that the rejections of record are clearly not proper and that the claims currently pending are distinguishable from the references cited and are in condition for allowance. Applicants respectfully request that a Notice of Allowability be issued in this case. If the Examiner wishes to discuss any aspect of this response, please contact the undersigned at the telephone number indicated below.

Respectfully submitted,

/John F. Kane/

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